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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/696,162	SINGH, SUJAY	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 13-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed July 3, 2006. Applicant's response to restriction requirement of May 30, 2006 has been entered. No claims were cancelled or newly added.

Claims 1-49 are pending in the application.

Election/Restrictions

Applicant's election of Group I (claims 1-12), without traverse, drawn to a transgenic vertebrate mammal whose genome comprises a bacteriophage RNA polymerase transgene, is acknowledged. Applicant's oral election of mouse, as the species of mammal is further acknowledged (see interview summary). The election requirement between the species of RNA polymerase is withdrawn. Claims 2-4 and 13-49 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions. The requirement for restriction is still deemed proper, maintained and hereby made FINAL.

Applicant timely responded to the restriction (election) requirement in the Paper filed July 3, 2006. Claims 1, and 5-12 are currently under examination.

Claim Objections

Claims 1, and 5-12 are objected to because of the following informalities: the claims have not been amended to recite the elected species or transgenic mouse, and encompass non-elected subject matter, i.e. a broad variety of transgenic vertebrates. Appropriate correction is required.

Claim Rejections - 35 USC § 101-Lack of Utility

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.
B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)
C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".
D. A method of making a material that itself has no specific, substantial, and credible utility.
E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an

enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP § 2107 - 2107.02.

Claims 1, and 5-12 are rejected under 35 U.S.C.§ 101 because the claimed invention is not supported by either a specific or substantial asserted utility.

The claims encompass a transgenic mouse whose genome comprises a bacteriophage RNA polymerase as a transgene that is capable of being expressed in at least one cell of said transgenic vertebrate.

The instant specification discloses a prophetic example of producing a transgenic mouse expressing T7RNA polymerase under the control of the constitutive CMV promoter (Example I, pp. 33-34). The specification further describes the introduction of sequences to be expressed in said transgenic mouse for antibody production (Examples 2 and 3, pp. 34-37).

However, none of the asserted utilities of the knockout animals, appear specific and substantial, because a transgenic mouse whose genome comprises a bacteriophage RNA polymerase does not provide for the production of antibodies that cannot be produced in a wild type mouse co-transfected with a sequence of interest and RNA polymerase. At the time of the claimed invention, one skilled in the art (Artisan) would not have found such utilities for the instantly claimed mouse as specific, because the art clearly establishes the production of antibodies in all mice. The specification further states: "Co-transfection of plasmid expressing T7 RNA polymerase and a plasmid containing a gene downstream of a T7 RNA polymerase promoter can be used to express foreign genes in a mouse. This system has been shown to achieve rapid and high levels of gene expression in a variety of animal cells and tissues. (first paragraph, p. 10). This methodology has been described in the prior art of Selby et al. (U.S.

Patent No. 6,355,247, Mar. 12, 2002), teaching a method for nucleic acid immunization to generate CTLs against an antigen comprising introducing a source of bacteriophage T7 RNA polymerase into a cell of a vertebrate subject (claim 1).

As the production of antibodies may be carried out in any mouse, in order to determine a specific utility for the mice of the instant invention, the Artisan of skill would need to perform further research upon the claimed mice, to determine whether any advantage regarding antibody production may be achieved over other non-genetically modified mice. As set forth in the utility guidelines above, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient, absent a disclosure of what condition can be diagnosed. Similarly, a statement of general utility for antibody production is non-specific, renders the purported utility of the claimed mice to be non-specific. The usefulness of the transgenic mice, as organisms for general antibody production, is not clear. The utility guidelines further state that a claim to an intermediate product for use in making a final product that has no specific utility does not define a real world use, or a substantial utility. This leaves the Artisan of skill to speculate the uses of the mice, as claimed. Under the utility guidelines set forth above, requirement for further research or experimentation renders the claimed invention as lacking in a specific or substantial utility. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real-world" context of use are not considered substantial utilities. The evidence of record has not provided any other utilities for the transgenic mice encompassed by the claims that are substantial and specific.

Because the mice have no determined specific function, having no distinguishing phenotype from wild type mice, the Artisan, at the time of filing, would not know how to use the mice without further experimentation. In light of the above, the Artisan of skill would not find the asserted utility of the transgenic mice encompassed by the claims to be specific and substantial.

Claim Rejections - 35 USC § 112 - Lack of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, and 5-12 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claimed invention is not supported by a specific utility or substantial utility for the reasons set forth above.

The specification is not enabling for a transgenic mouse whose genome comprises a bacteriophage RNA polymerase, having no distinguishing phenotype from a wild type mouse, as claimed, because one skilled in the art clearly would not know how to use the claimed invention, without further experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 5-12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Selby et al. (U.S. Patent No. 6,355,247, Mar. 12, 2002), in view of Wirtz et al. (Nucl. Acids Research 22:3887-3894; 1994).

Selby et al. describe a method for nucleic acid immunization to generate CTLs against an antigen comprising introducing a source of bacteriophage T7 RNA polymerase into a cell of a vertebrate subject (claim 1). Selby et al. state: "the T7 RNA polymerase gene will be operably linked to regulatory sequences recognized by the particular host, or even particular cells within the host. Thus, eukaryotic and phage regulatory sequences will generally be present for expression in mammalian hosts. Such regulatory sequences are known in the art and include but are not limited to promoters derived from SV40, CMV, HSV, RSV, MMTV" (column 11).

Promoters such as SV40 and MMTV are constitutive promoters, whereas MMTV is an inducible promoter. The system described is intended for use in vertebrate species, that include rodents such as mice (column 6). Therefore, Selby et al. describe a nucleic acid immunization system using mice that express T7 RNA polymerase, providing controlled, transient expression of a given antigen and which elicit the production of class I MHC restricted CTLs (Abstract). While Selby et al. do not specifically describe a transgenic animal whose genome comprises a bacteriophage RNA polymerase as a transgene, they state: "Accordingly, T7 RNA polymerase is provided either prior, subsequent or concurrent with administration of the nucleic acid of interest" (last paragraph, column 10).

Wirtz et al. describe gene expression mediated by bacteriophage T3 and T7 RNA polymerase in transgenic trypanosomes (Title). The transgenic *Trypanosoma brucei* are described as stably expressing functional, nuclearly localized T3 or T7 RNA polymerase, having from one half to greater than five times greater promoter driven expression than endogenous pol I (Abstract). Wirtz et al. state: "We have shown that in trypanosomes, genes under the control of phage promoters are transcribed by introduced T3 and T7 RNA polymerase, trans-spliced, and translated with an efficiency that leads to very high –level expression. Hence, the usual eukaryotic link between mRNA production and RNA polymerase II can indeed be by-passed in trypanosomes by these phage polymerases" (first column, p. 3893). Therefore, it would have been *prima facie* obvious to someone of ordinary skill in the art at the time of the instant invention to combine the transgenic bacteriophage RNA polymerase expression system of Wirtz et al. with the mammalian, vertebrate or mouse system of Selby et al., to establish stable transgenic RNA polymerase expression, as the expression system of Selby et al. is transient (Abstract), thus further providing for the transgenic RNA polymerase to be present prior to administration of nucleic acid of interest, as also suggested by Selby et al.

Therefore, a person of ordinary skill in the art, would have been motivated to combine the transgenic bacteriophage RNA polymerase expression of Wirtz et al. together with the T7 RNA polymerase mediated system described by Selby et al., because the stable expression and presence of the bacteriophage RNA polymerase in a transgenic animal that is a mouse would allow the production of a CTL response to an introduced foreign antigen and would have a

reasonable expectation of success in producing a transgenic mouse whose genome comprises a bacteriophage RNA polymerase as a transgene.

Hence, the claimed invention a whole is *prima facie* obvious, absent evidence to the contrary.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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